

AMENDMENTS TO THE CLAIMS

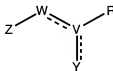
The following listing of the claims will replace all prior versions, and listings, of claims in the application:

1. (Currently amended) A method of inhibiting the GTPase activity of dynamin activity in a cell or synaptosome, comprising contacting a cell or synaptosome dynamin-with an effective amount of a compound of formula I, or a physiologically acceptable salt thereof, to inhibit said GTPase activity in said cell or synaptosome, wherein



Formula I

M and M' are each independently a moiety of formula II and are the same or different, and Sp is a spacer comprising a 1 to 7 atom chain;



Formula II

V is C or CH;

W is CH or a linker group of up to 3 atoms in length; and

Y is cyano, nitro, NH, amino, oxo, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy, sulfur, or an unsubstituted C₁-C₃ group or C₁-C₃ group substituted with at least one group independently selected from cyano, nitro, NH, amino, oxo, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy and sulfur; or

W, V and Y form a 5 or 6 membered substituted or unsubstituted heterocyclic or carbocyclic ring fused with Z, wherein the heterocyclic ring includes from 1 to 3 heteroatoms selected from O, N and S, and the heterocyclic or carbocyclic ring, when

substituted, has at least one substituent selected from cyano, nitro, NH, amino, oxo, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy, sulfur, or an unsubstituted C₁-C₃ group or C₁-C₃ group substituted with at least one group independently selected from cyano, nitro, NH, amino, oxo, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy and sulfur; and

R is CH₂R', CXR' or CHX'R';

X is O or S;

X' is cyano, nitro, amino, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy, or an unsubstituted C₁-C₃ group or C₁-C₃ group substituted with at least one group independently selected from cyano, nitro, NH, amino, oxo, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy and sulfur;

R' is NH, O or S bonded to the spacer; and

Z is selected from:

(a) ~~an unsubstituted heterocyclic group consisting of one or two rings independently having 5 or 6 ring members including up to 3 heteroatoms selected from O, N and S;~~

(b) ~~an unsubstituted carbocyclic group consisting of one or two rings independently having 5 or 6 ring members;~~

(c) ~~a heterocyclic group consisting of one or two rings independently having 5 or 6 ring members including up to 3 heteroatoms selected from O, N and S wherein the heterocyclic group has one or more substituents independently selected from:~~

(i) ~~nitro, NH, amino, cyano, halo, hydroxy, carboxy, oxo, sulfur, sulfhydryl, C₁-C₂ alkoxy and C₁-C₂ acyl; and~~

(ii) ~~a C₁-C₂ alkyl or C₁-C₂ alkenyl group with at least one substituent selected from nitro, NH, amino, cyano, halo, hydroxy, carboxy, oxo, sulfur, sulfhydryl, C₁-C₂ alkoxy and C₁-C₂ acyl; and~~

(d) ~~a carbocyclic or heterocyclic group, consisting of one or two rings ring independently having 5 or 6 ring members[.]] and at least two substituents when W is CH or a linker group or W, V and Y form an unsubstituted carbocyclic group, or at least one substituent when W, V and Y form a heterocyclic group, independently selected from[[:]]~~

(i)—nitro, NH, amino, cyano, halo, hydroxy, carboxy, oxo, sulfur, sulfhydryl, C₁-C₂ alkoxy, ~~and~~ C₁-C₂ acyl₃, ~~and~~

(ii)—~~or~~ a C₁-C₂ alkyl or C₁-C₂ alkenyl group with at least one substituent selected from nitro, NH, amino, cyano, halo, hydroxy, carboxy, oxo, sulfur, sulfhydryl, C₁-C₂ alkoxy and C₁-C₂ acyl[[:]]

~~wherein when Z of one of M or M' is selected from (b), Z of the other of M or M' is selected from (a), (c) or (d).~~

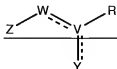
2-25. (Cancelled)

26. (Currently amended) [[A]] The method of claim 1, wherein the method inhibits a dynamin-dependent condition in a mammal prophylaxis or therapeutic treatment of a disease or condition in a mammal mediated by dynamin-dependent endocytosis, the method comprising administering to the mammal an effective amount of a compound of Formula I, or a physiologically acceptable salt, or prodrug thereof, wherein:



Formula I

~~M and M' are each independently a moiety of formula II and are the same or different, and Sp is a spacer;~~



Formula II

V is C or CH;

W is CH or a linker group; and

Y is cyano, nitro, NH, amino, oxo, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy, sulfur, or an unsubstituted C₁-C₃ group or C₁-C₃ group substituted with at least one group independently selected from cyano, nitro, NH, amino, oxo, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy and sulfur; or

W, V and Y form a 5- or 6-membered substituted or unsubstituted heterocyclic or carbocyclic ring fused with Z_n wherein the heterocyclic ring includes from 1 to 3 heteroatoms selected from O, N and S, and the heterocyclic or carbocyclic ring, when substituted, has at least one substituent selected from cyano, nitro, NH, amino, oxo, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy, sulfur, or an unsubstituted C₁-C₃ group or C₁-C₃ group substituted with at least one group independently selected from cyano, nitro, NH, amino, oxo, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy and sulfur; and

R is CH₂R', CXR' or CHX'R';

X is O or S;

X' is cyano, nitro, amino, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy, or an unsubstituted C₁-C₃ group or C₁-C₃ group substituted with at least one group independently selected from cyano, nitro, NH, amino, oxo, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy and sulfur;

R' is NH, O or S bonded to the spacer; and

Z is selected from:

(a) — an unsubstituted heterocyclic group consisting of one or two rings independently having 5 or 6 ring members including up to 3 heteroatoms selected from O, N and S;

(b) — an unsubstituted carbocyclic group consisting of one or two rings independently having 5 or 6 ring members;

(c) — a heterocyclic group consisting of one or two rings independently having 5 or 6 ring members including up to 3 heteroatoms selected from O, N and S wherein the heterocyclic group has one or more substituents independently selected from:

(i) — nitro, NH, amino, cyano, halo, hydroxy, carboxy, oxo, sulfur, sulfhydryl, C₁-C₂ alkoxy and C₁-C₂ acyl; and

(ii) — a C₁-C₂ alkyl or C₁-C₂ alkenyl group with at least one substituent selected from nitro, NH, amino, cyano, halo, hydroxy, carboxy, oxo, sulfur, sulfhydryl, C₁-C₂ alkoxy and C₁-C₂ acyl; and

(d) — a carbocyclic group consisting of one or two rings independently having 5 or 6 ring members, and at least two substituents when W is CH or a linker group or W, V and Y form an unsubstituted carbocyclic group, or at least one substituent when W, V and Y form a heterocyclic group, independently selected from:

(i) — nitro, NH, amino, cyano, halo, hydroxy, carboxy, oxo, sulfur, sulfhydryl, C₁-C₂ alkoxy and C₁-C₂ acyl; and

(ii) — a C₁-C₂ alkyl or C₁-C₂ alkenyl group with at least one substituent selected from nitro, NH, amino, cyano, halo, hydroxy, carboxy, oxo, sulfur, sulfhydryl, C₁-C₂ alkoxy and C₁-C₂ acyl;

wherein when Z of one of M or M' is selected from (b), Z of the other of M or M' is selected from (a), (c) or (d).

27-55. (Cancelled)

56. (Currently amended) A method according to claim 26, wherein for at least one of M and M':

V is C;

W is CH; and

Y is cyano, nitro, amino, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy, or an unsubstituted C₁-C₂ group or C₁-C₂ group substituted with at least one group independently selected from cyano, nitro, NH, amino, oxo, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy and sulfur; or

W, V and Y form a 5 or 6 membered substituted or unsubstituted heterocyclic or carbocyclic ring fused with Z, wherein the heterocyclic ring includes from 1 to 3 heteroatoms selected from O, N and S, and the carbocyclic or heterocyclic ring, when

substituted, has at least one substituent selected from cyano, nitro, NH, amino, oxo, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy and sulfur, or an unsubstituted C₁-C₂ group or C₁-C₂ group substituted with at least one group independently selected from cyano, nitro, NH, amino, oxo, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy and sulfur; and

R is CH₂R', CXR' or CHX'R';

X is O or S; and

X' is cyano, nitro, amino, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy, or an unsubstituted C₁-C₂ group or C₁-C₂ group substituted with at least one group independently selected from cyano, nitro, NH, amino, oxo, halo, hydroxy, sulfhydryl; carboxy, thiocarboxy and sulphur.

57. (Currently amended) A method according to claim 56, wherein:

Y is cyano, nitro, amino, carboxy, hydroxy, sulfhydryl, or thiocarboxy; or

W, V and Y form a 5 or 6 membered substituted or unsubstituted heterocyclic or carboxylic ring fused with Z, wherein the heterocyclic ring includes from 1 to 3 heteroatoms selected from O, N and S, and the carbocyclic or heterocyclic ring, when substituted, has at least one substituent selected from cyano, nitro, amino, hydroxy, sulfhydryl, carboxy and thiocarboxy, or a C₁-C₂ group substituted with a group selected from cyano, nitro, amino, hydroxy, sulfhydryl, carboxy and thiocarboxy; and

R is CXR'.

58. (Currently amended) A method according to claim 57, wherein the Z group is selected from:

~~a heterocyclic group consisting of one or two rings independently having 5 or 6 ring members including up to 3 heteroatoms independently selected from O, N and S;~~

~~a heterocyclic group consisting of one or two rings independently having 5 or 6 ring members including up to 3 heteroatoms independently selected from O, N and S, wherein the heterocyclic group has one or more substituents independently selected from nitro, NH, halo, cyano, amino, hydroxy, carboxy, oxo, sulfur, and C₁-C₂ alkoxy; and~~

an ~~a~~ carbocyclic group consisting of one or two rings independently having 5 or 6 ring members, and at least two substituents independently selected from nitro, NH, amino, halo, cyano, hydroxy, carboxy, oxo, and sulfur and C_1-C_3 alkoxy.

59. (Cancelled)

60. (Currently amended) A method according to claim 58, wherein the Z group is an aryl group with has:

~~at least two of said substituents in ortho positions relative to one another on a said ring of Z, when the Z group is a carbocyclic group; or~~

~~a substituent on a carbon atom adjacent to a heteroatom of a said ring of Z, when the Z group is a heterocyclic group; or~~

~~when W, V and Y are cyclised forming a heterocyclic ring fused with Z, a substituent on a carbon atom of a said ring of the Z group, the carbon atom being at least one bond length from the heterocyclic ring formed by W, V, and Y.~~

61. (Currently amended) A method according to claim 60, wherein W, V and Y form a 5 or 6 membered heterocyclic or carbocyclic ring fused with Z the Z group consists of a single aryl side ring of 5 or 6 members.

62. (Currently amended) A method according to claim [[61]] 60, wherein ~~W, V and Y~~ forms a 6 membered heterocyclic ring fused with Z.

63. (Currently amended) A method according to claim 61 wherein V is C_1 , W is CH and Y is cyano, nitro, amino, carboxy, hydroxy, sulfhydryl or thiocarboxy.

64. (Currently amended) A method according to claim 58, wherein the Z group is an aryl group with ~~consisting of one or two rings independently having 5 or 6 ring members, and at least two substituents in ortho positions relative to one another, wherein said substituents are~~ independently selected from nitro, NH, amino, ~~halo~~, cyano, hydroxy, carboxy, oxo[[,]] and

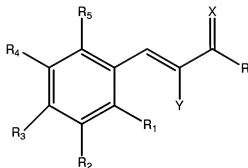
sulphur and C_1 - C_2 alkoxy.

65. (Currently amended) A method according to claim 64_a wherein the ~~Z group is a phenyl group having 6 ring members and at least two substituents~~ are independently selected from nitro, amino, halo, cyano, and hydroxy, carboxy and C_1 - C_2 alkoxy.

66. (Currently amended) A method according to claim 65_a wherein the ~~phenyl group has at least two substituents independently selected from nitro, amino, carboxy and~~ are hydroxy.

67-68. (Cancelled)

69. (Currently amended) A method according to claim 26_a wherein M and M' are each independently a moiety as follows:



wherein[[:]] X is O or S ;

Y is cyano, nitro, amino, halo, hydroxy, sulfhydryl, carboxy, or thiocarboxy; or

R₁ and Y are cyclised forming a 5 or 6 membered substituted or unsubstituted heterocyclic or carbocyclic ring, wherein the heterocyclic ring includes 1 or 2 heteroatoms selected from O, N and S, and the carbocyclic or heterocyclic ring, when substituted, has at least one substituent selected from cyano, nitro, NH, amino, oxo, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy and sulfur; and

R₂ to R₅ are independently hydrogen or a substituent independently selected from nitro, amino, halo, hydroxy, carboxy, sulfhydryl, thiocarboxy, C₁-C₂ alkoxy and C₁-C₂ acyl; or

R₁ to R₅ are independently hydrogen or a substituent independently selected from nitro, amino, halo, hydroxy, carboxy, sulfhydryl, thiocarboxy, halo, C₁-C₂ alkoxy and C₁-C₂ acyl; and

R is NH, O is S bonded to the spacer Sp; and

wherein at least one of M and M' is characterised in that, at least two of R₁ to R₅ are other than hydrogen, and when R₁ to R₂ are other than hydrogen at least one of R₃ to R₅ is also other than hydrogen, or when R₁ and Y are cyclised, at least two of R₂ to R₅ are other than hydrogen ~~when R₁ and Y form an unsubstituted carbocyclic group or at least one of R₂ to R₅ is other than hydrogen when Y and R₁ form a heterocyclic group.~~

70. (Currently amended) A method according to claim 69, wherein at least two of [[R₁]] R₂ to [[R₅]] R₄ are other than hydrogen.

71. (Cancelled)

72. (Currently amended) A method according to claim [[71]] 70, wherein at least three of R₁ to [[R₅]] R₄ are other than hydrogen ~~and are in adjacent substitution positions to one another.~~

73. (Currently amended) A method according to claim [[72]] 70, wherein at least two of R₂ to R₄ are hydroxy.

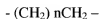
74. (Cancelled)

75. (Currently amended) A method according to claim 73, wherein Y is cyano, X is O and R is NH.

76. (Currently amended) A method according to claim 75, wherein M and M' are the same.

77. (Currently amended) A method according to claim 26, wherein the spacer Sp permits the compound to adopt a hairpin conformation.

78. (Currently amended) A method according to claim 26, wherein the spacer Sp comprises an unsubstituted alkane chain as follows:



wherein n is an integer of from 1 to 5.

79. (Currently amended) A method according to claim 1, wherein the compound of Formula I is a dimeric tyrphostin.

80. (Cancelled)

81. (Previously presented) A method according to claim 73, wherein X is O, R is NH and R₁ and Y are cyclised, forming a substituted heterocyclic group with 6 ring members.

82-85. (Cancelled)

86. (Currently amended) The method of claim 26, wherein the method prevents or treats epilepsy or inhibits a dynamin-dependent endocytosis in a mammal, the method comprising administering to the mammal according to claim 1 being a method for inhibiting dynamin-dependent endocytosis in cells, the method comprising treating the cells with an effective amount of the compound of formula I, or a physiologically acceptable salt or prodrug thereof,